

Diagnosis of Lassa fever and the isolation and management of patients

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The clinical spectrum of Lassa fever is described and discussed in terms of the possible pathophysiological events involved. Early diagnosis is essential to permit prompt isolation of the potentially infectious patient. Lassa fever may be suspected on clinical grounds, but specific early diagnosis depends upon isolation of the virus. Virus isolation is best accomplished from serum obtained during the first 2 weeks of illness. The patterns of viraemia and virus excretion described in this paper are useful guidelines for determining the duration of patient isolation. Problems encountered in the isolation, management, and transport of the patient with Lassa fever are discussed.

Lassa virus infection in man may be followed by a spectrum of disease that varies from a mild acute febrile illness of brief duration to a prolonged fatal disease with severe toxæmia, capillary leakage, haemorrhagic phenomena, shock, and dysfunction of many organ systems. Establishing a clinical diagnosis at an early stage is especially important because of the transmissibility of infection from person to person and the need for effective isolation of the patient and for containment of potentially infectious specimens during virological and clinico-pathological testing.

In this paper we attempt to review the clinical features of Lassa fever in relationship to the presumed pathophysiological events involved and to provide a basis for clinical diagnosis and therapeutic management. In addition, the patterns of viraemia and virus excretion are described in order to formulate measures for isolating the patient.

CLINICAL FEATURES

The symptomatology of Lassa fever is often non-specific, especially early in the disease, and consequently the diagnosis may be difficult until multiple similar cases appear in the setting of an epi-

demic or until the consummate and severe clinical syndrome becomes apparent in an individual patient.

The incubation period is generally between 7 and 10 days, but may be as short as 3 days or as long as 17. A prodrome has not been defined, but the onset of illness is usually insidious rather than sudden. The acute phase has lasted 2 to 4 weeks in patients who have entered hospital, but is probably shorter in mild cases escaping medical attention. The frequency of symptoms and signs is shown in Table 1 and the chronology in Fig. 1. Initial symptoms include feverishness, chills, generalized malaise, diffuse muscle aching, and headache. During the first week other symptoms that may be present include sore throat, dysphagia, nausea, vomiting, diarrhoea, cough, and pains in the chest and abdomen. Diarrhoea tends to cease at the end of the first week, whereas other gastrointestinal symptoms (abdominal pain and vomiting) may persist into the second week of illness. Chest pain, often pleuritic in nature, increases in intensity during the first week and may be present during the second and third weeks. Dizziness, tinnitus, and unilateral or bilateral hearing loss are less frequent and later symptoms appearing during the second week of illness.

On physical examination, the patient is febrile, appears toxic, and may be dehydrated. The blood and pulse pressures are low, and there may be a slower pulse than is normal with fever. Abnormal signs include conjunctival inflammation; coated tongue; lymphadenopathy; exudative pharyngitis;

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Table 1. Lassa fever; frequency of symptoms and signs in patients observed during epidemics at Jos, Nigeria (1970), Zorzor, Liberia (1972), and Panguma, Sierra Leone (1972).

Symptom	Frequency (%) ^a	Sign	Frequency (%) ^a
nausea/vomiting	80	fever	100
sore throat	80	pharyngitis	79
cough	68	reduced blood pressure and pulse pressure	66
headache	57	abdominal tenderness	53
abdominal pain	57	lymphadenopathy	48
myalgia	46	puffiness of face or neck	36
diarrhoea	43	coated tongue	36
chest pain	39	conjunctivitis	34
dizziness	25	bleeding	32
deafness	18	rales	25
tinnitus	16	muscle tenderness	21
constipation	5	petechiae	12
		rash	7
		convulsions	5
		leukopenia (<4000/mm ³)	41
		albuminuria (≥2+)	52

^a Based on 34-44 patients; denominator variable because of incomplete recording of information on specific symptoms or signs.

pulmonary rales; tenderness of intercostal, lumbar, or other muscles; abdominal tenderness (particularly over the liver) and, occasionally, a maculopapular rash. Pharyngitis has been noted in approximately 80% of the cases and is characterized by patchy exudates varying in size from 1 mm to a coalescent pseudomembrane. Dizziness has been associated with nystagmoid eye movements in one case (1), but nystagmus has been absent in others. Hearing loss is demonstrable on gross examination. Jaundice has not been reported. Spiking low-grade fevers with no definite pattern have been noted in surviving cases (2); high persistent fever appears to correlate with severe disease and a poor prognosis. In surviving cases, fever breaks by lysis as symptoms and signs gradually subside between the second and fourth weeks of illness.

Convalescence may be accompanied by complaints of generalized weakness lasting several weeks. After a severe infection, one patient had prolonged generalized neurologic dysfunction, with tremulousness, involuntary eye movements, un-

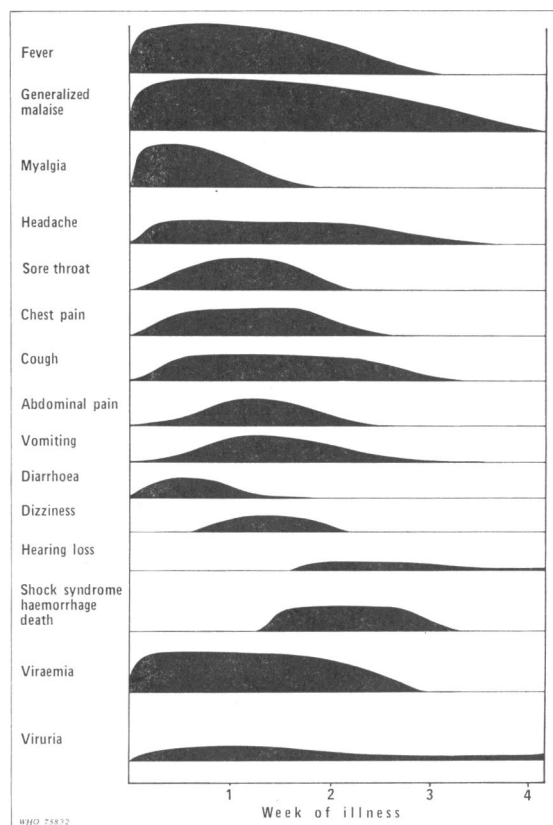


Fig. 1. Diagrammatic scheme of the chronology of symptoms of Lassa fever.

steady gait, and episodic dizziness (1). Deafness developing during the acute illness has been irreversible in some patients. Loss of scalp hair during the convalescent period has not been infrequent. Two instances of relapse of fever and symptoms have been reported (2, 3).

In 35-50% of hospitalized cases the disease may progress to its severe form, with persistent high fever, signs of increasing toxicity, diffuse capillary leakage, a haemorrhagic diathesis, central nervous system disturbances, respiratory distress, oliguria, and shock. Such cases tend to have a fatal outcome, generally in the second week of illness. Capillary leakage is manifested by the appearance of serous effusions, oedema of the face and neck, petechiae, rales, and haemodynamic instability.

Respiratory distress has been associated with severe Lassa fever in several settings: (a) airway obstruction by cervicofacial, pharyngeal, or laryngeal oedema; (b) pleural effusions with or without

painful pleuritis, which cause a reduction in lung volumes; (c) pulmonary oedema, congestion, atelectasis, or haemorrhage associated with a diffuse capillary leak syndrome and shock; (d) dyspnoea due to arterial acidemia; and (e) congestive heart failure due to overhydration in the face of diminished renal function and/or myocarditis.

Metabolic acidosis, though for technical reasons not yet documented, is almost certainly an important pathophysiological event in patients with severe Lassa fever and shock. The difficulty in management of acidosis and attendant serum potassium imbalance without the benefit of blood gas analysis has probably contributed to the high mortality of Lassa fever in Africa.

Renal failure has been noted in severely ill patients who develop shock, possibly due both to reduced renal perfusion and to direct viral injury. Development of acute tubular necrosis has not been recognized, since patients have not survived the development of shock.

Haemorrhage, which has taken the form of ecchymoses and oozing from needle puncture sites and minor gastrointestinal bleeding, has not been clinically important.

CNS disturbances have been quite striking in some cases and include tremor, alterations in consciousness, and generalized convulsions. Cerebrospinal fluids have shown no abnormalities. These encephalopathic manifestations have coincided with profound physiological alterations in other organ systems and probably systemic metabolic derangements; without further study they cannot be considered as primary results of Lassa virus infection. The localizing neurological signs noted in an outbreak (not confirmed as Lassa fever) in Sierra Leone in 1956 (4) have not been described in reports of subsequent epidemics.

Characteristically, the body temperature falls to subnormal levels an hour or more before death.

CLINICAL PATHOLOGY

Clinical laboratory examinations may be of diagnostic aid, either in helping to establish other etiologies or in supporting the suspicion of Lassa fever. It should be emphasized that the information at present available is derived from studies on a few hospitalized, severely ill patients.

A moderate leukopenia has been noted early in the disease, especially between the fourth and tenth days (Table 2), but absence of a low white cell count

Table 2. White blood counts in patients with Lassa fever

Time after onset (days)	Number of determinations with white cell count of		
	2000-2500 (wbc/mm ³)	2501-4000 (wbc/mm ³)	>4000 (wbc/mm ³)
0-3	1		4
4-7	3	5	4
8-10	1	6	8
11-14		1	5
15+			6

is not a helpful diagnostic criterion. Late in illness, a marked leukocytosis may occur. Abnormalities in the platelet count, prothrombin time, and clotting times sometimes occur (9, 10). Increased amounts of albumin in the urine and abnormal urinary sediment (cells and granular casts) have been reported in approximately half of the patients, especially in severe or fatal cases (9).

Elevations of serum enzymes (creatinine phosphokinase, lactic dehydrogenase, and glutamic-oxaloacetic transaminase) have been found in a few cases. These changes are nonspecific and may reflect damage to the liver, myocardium, and/or skeletal muscle.

The cerebrospinal fluid has been normal (1, 3).

Electrocardiographic examinations have been infrequently made; conduction defects, ST-T wave changes, and abnormal Q waves have been described (10, 11), suggesting myocardial injury. In several instances, the chest X-ray has shown infiltrates consistent with pneumonitis (1).

PATHOPHYSIOLOGICAL CORRELATIONS

The pathology of human Lassa virus infection has been reviewed by Winn & Walker during this Symposium (5) and by previous authors (1, 6, 7, 8). The pathophysiological alterations in severe Lassa fever remain obscure and are certainly complex. Clinical observations suggest that alterations in capillary permeability, possibly due to direct viral injury, pharmacological mediators, or complement split products, may be a central event. A schematic representation of the presumed pathophysiological mechanisms is shown in Fig. 2.

Secondary results of capillary leakage and reduced effective circulating blood volume may include increase in sympathetic tone, local tissue acidosis and anoxia, and further reduction in tissue blood flow, thus generating the shock syndrome. Pre-renal fail-

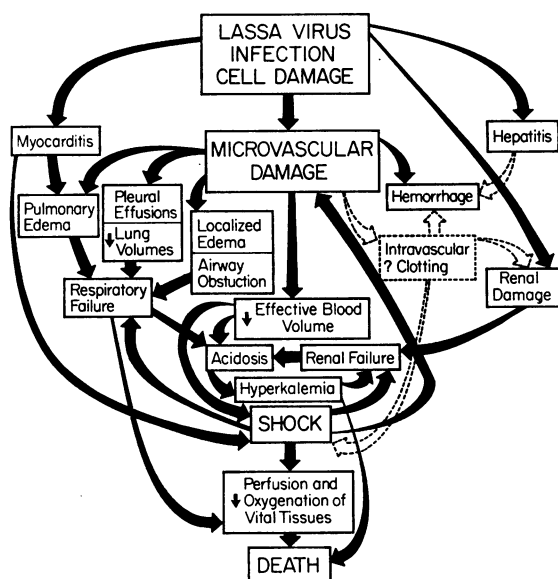


Fig. 2. Hypothetical mechanisms involved in the pathophysiology of Lassa fever infection.

ure, lactic acidemia, hyperkalemia, and reduced perfusion and oxygenation of vital tissues ensue and progress to a fatal outcome. Other secondary effects of microvascular damage include alterations in pulmonary function due to several mechanisms. Respiratory failure may contribute to the anoxia and acidosis associated with the shock syndrome. Disseminated intravascular coagulation has not been confirmed by laboratory tests, but may play a role in the haemorrhagic diathesis, renal damage, and the generation of shock. In addition to the secondary effects, direct viral damage to vital organs, such as the liver (5-8), heart, and kidney, play an undetermined role in the pathogenesis of the severe syndrome.

Since both the haemodynamic and metabolic disturbances may be amenable to specific therapeutic measures, future efforts should be directed towards documentation of these abnormalities in the patient. The lack of relatively advanced monitoring equipment makes such studies difficult in hospitals in remote rural areas.

CLINICAL AND DIFFERENTIAL DIAGNOSIS

The diagnosis of Lassa fever must be seriously considered for a patient living in or travelling from endemic areas of West Africa who presents with the triad of fever, exudative pharyngitis, and a low or

slightly subnormal white cell count. Streptococcal pharyngitis and viral illness due to adenoviruses, coxsackieviruses, and herpesvirus generally have a sudden onset and a briefer febrile course (less than 3-4 days). Diphtheria must be considered when pharyngeal lesions are severe. Bacteriological examination of the throat and measurement of the peripheral white blood count may be useful in differentiating infections due to bacterial organisms.

Fever lasting more than 3-4 days accompanied by pulmonary symptoms (cough, pleurisy, effusions) and signs may suggest viral, chlamydial, or bacterial pneumonia. Examination of the sputum, chest X-ray, white blood count, and response to antimicrobial therapy may assist in the diagnosis. Tuberculosis, relapsing fever, pulmonary infarction, and other diagnoses may also be considered.

Fever, lumbar pain and tenderness, and gastrointestinal symptoms may mimic acute pyelonephritis. The demonstration of bacteria and numerous leukocytes in the urine, a polymorphonuclear leukocytosis, and a response to antibiotic therapy are helpful in distinguishing this disease from Lassa fever.

Blood smears should be examined for malaria parasites, but it is emphasized that the presence of plasmodia does not exclude concurrent infection with Lassa virus; antimalarials may be administered routinely as a therapeutic trial.

A number of diseases (e.g., typhoid, early infectious hepatitis, influenza, yellow fever, dengue, infectious mononucleosis, leptospirosis, relapsing fever, typhus, and rheumatic fever) may produce a clinical picture resembling that of Lassa fever. Similarities between Lassa and typhoid fevers include insidious onset, prolonged fever, headache, rash, lymphadenopathy, relative bradycardia, gastrointestinal symptoms, cough, leukopenia, sore throat, vascular collapse, hypothermic death, and residual deafness. Culture of the blood (if available) during the first week of illness may be extremely helpful in the diagnosis of typhoid; response to chloramphenicol may distinguish the disease.

VIROLOGICAL AND SEROLOGICAL DIAGNOSIS

Specific diagnosis requires isolation and identification of the virus or demonstration of an antibody rise using paired serum samples.

The pattern of viraemia and virus excretion in patients studied to date (Fig. 3), provides guidelines both for attempts at early virological diagnosis and for instituting and continuing the isolation of pa-

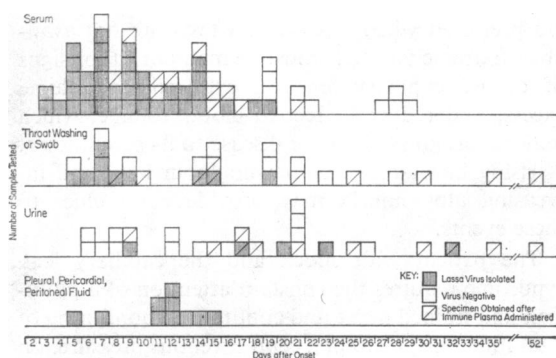


Fig. 3. Results of virus isolation attempts from serum, throat swabs, urine, and other body fluids obtained from Lassa fever patients studied between 1969 and 1974.

tients. Virus isolations are best accomplished from serum collected within 14 days from onset. Of 44 sera collected during this period, 36 (82%) were positive; 6 of the 8 negative sera were obtained from patients who had been transfused with Lassa immune plasma shortly before. The longest documented viraemia is 19 days.

Virus has been isolated from approximately half of the throat washings or swabs tested during the first 14 days of illness. The duration of pharyngeal excretion parallels the viraemia. In 2 patients who received transfusions of immune plasma, viraemia ceased but throat washings remained positive (2, 10).

Viruria has been less frequently demonstrated, but it may be present for more prolonged periods despite the administration of immune plasma (Fig. 3).

Present constraints on the early specific diagnosis of Lassa fever by virus isolation include: (1) the time and practical obstacles encountered in the shipment of specimens from West Africa to a diagnostic laboratory with biocontainment facilities and (2) the time required in the laboratory for demonstration of the virus.

Serological diagnosis by conversion of the complement-fixation (CF) test from negative to positive in paired serum samples is not an efficient means of establishing an early diagnosis. Of 29 sera taken between days 3 and 14 after onset from patients whose diagnosis was proved by virus isolation or serological conversion, only 3 (10%) were CF-positive; and of 28 sera taken between days 15 and 28, 19 (68%) were positive. The presence of CF antibody in serum has been demonstrated in patients from whom virus was simultaneously recovered from the pharynx (2).

The indirect fluorescent antibody (IFA) test is apparently more sensitive than the CF test and may detect antibody earlier following infection. Further studies are required.

ISOLATION OF THE PATIENT

The principles and practice of isolation are beyond the scope of this paper and may be found in a US Government publication, which is readily available (12). Once the clinical suspicion of Lassa fever is entertained, the physician must turn to account his understanding of the source of infection and routes of transmission of Lassa virus (13) in order to adapt the ideal principles of isolation to the more limited local capabilities. Procedures within the capabilities of many, though certainly not all, hospitals in West Africa include the use of a private room and toilet facility, protection of staff against contact spread by the use of gowns, gloves, and masks, and disinfection of objects coming in contact with the patient.

To date Lassa virus has not been transmitted from a patient *in isolation* to a medical attendant or visitor. Although routine isolation techniques are probably effective, one cannot be certain that they have prevented tertiary infections, since observations in the nosocomial outbreaks suggest that only the occasional patient is highly infectious (13-15).

In the setting of an epidemic, the physician is often faced with the problem of misdiagnosis when deciding to isolate a patient with symptoms and signs resembling, but not clinically diagnostic of, Lassa fever. Where facilities are limited, this decision may result in an exposure of an uninfected patient to Lassa virus. Whenever possible, patients with the questionable diagnosis of Lassa fever should be isolated in separate rooms rather than in an isolation ward. Where two or more patients must be isolated together, beds should be placed as far apart as possible (10-12 feet; 3-3.5 m), to minimize direct contact and droplet spread.

The duration of isolation cannot be rigidly specified. In practice, it will be determined by the length of time necessary for clinical recovery. Most patients will not feel well enough to be discharged until 3-4 weeks after onset, by which time viraemia and pharyngeal virus excretion will probably have subsided. Viruria may persist longer, and discharged patients should be advised of simple preventive measures to reduce the exposure of others to urine. For patients in hospitals with access to rapid virological analysis, the date of discharge may be deter-

mined by the cessation of virus excretion; viruria may be intermittent (2, 10), however, and sequential samples must be tested.

An unresolved problem is that of the safe handling of specimens for clinical diagnostic tests. Determination of haematological and chemical parameters may be helpful diagnostically, and certain tests (in particular, electrolytes and blood gases) may be essential to the care of the severely ill patient. In a few specialized centres, it may be possible to carry out the necessary clinical examinations in a virological laboratory or other laboratory with biocontainment facilities. This is not, however, a practical solution to the general problem.

For some determinations, clinical specimens can probably be rendered non-infectious. For example, the addition of blood to dilute acetic acid (20 mg/litre; pH 2.9) for leukocyte counting would be expected to inactivate Lassa virus. Blood smears used for differential cell counts or detection of malarial organisms can be fixed with glutaraldehyde. Although the thermal inactivation kinetics of Lassa virus have not been definitely measured, it appears that heating at 60°C for 1 hour is sufficient to inactivate the agent (H. Wulff, personal communication). Samples for measurement of electrolytes, creatinine, febrile agglutinins, or other thermostable components could thus be heated before they are used.

CLINICAL MANAGEMENT

Because of the uncertain prognosis for any patient in the early acute phase of Lassa fever, close observation is recommended in a hospital.

Supportive measures include bedrest, sedative analgesic drugs when required, paracetamol or tepid water-sponging to reduce fever and metabolic demands, and small amounts of viscous lidocaine swallowed to reduce sore throat when dysphagia is severe. Nausea and vomiting occur frequently and may require specific measures to relieve discomfort and reduce the risks of dehydration and electrolyte imbalance.

Vital functions, especially blood and pulse pressure, pulse, and intake and output, should be closely monitored. Serial measurements of haematocrit, urine specific gravity, and electrolytes, if available, will be useful in managing fluid balance. Dehydration or extracellular fluid volume depletion, which is present in a high proportion of cases, should be corrected and fluid balance maintained by appropriate fluid administration; the oral or rectal routes

are preferred when biochemical tests are not available. Extreme vigilance must be maintained for signs of diffuse capillary leakage, extracellular volume excess, and reduced effective blood volume, which indicate progression of the disease to its severe form. A rising haematocrit or haemoglobin level and increasing albuminuria may provide early clues to these events.

The patient with shock and the capillary leak syndrome requires the constant attention of a physician and trained nurse and continuous monitoring of vital functions, including central venous pressure, on a bedside flow chart. Administration of salt and water should be curtailed and a cautious attempt made to expand intravascular volume with colloids. The use of vasoactive drugs (isoprenaline, norepinephrine), digitalis, and diuretics (furosemide) may be indicated.

Respiratory distress is often apparent; its etiology should be ascertained (see *Clinical features*) and therapy guided accordingly.

Metabolic (lactic) acidosis and hyperkalaemia undoubtedly accompany the shock syndrome. Electrocardiographic monitoring may be helpful. Where blood gas analysis is not available, it may be prudent to administer bicarbonate on an empirical basis.

Corticosteroids have been used in the severely ill; no information is available regarding their efficacy (or possible deleterious effects) in Lassa fever. The use of pharmacological doses to counteract shock is still controversial.

Since intensive care facilities do not exist in regions where Lassa fever is endemic, emphasis should be placed on measures to reduce the factors contributing to the development of the shock syndrome. Correction of fluid balance during the early acute phase, and the administration of immune plasma, which may limit the extent of microvascular injury, are at present considered to be the most important measures.

SPECIFIC TREATMENT

Administration of plasma containing antibodies to Lassa virus has now been tried in a number of acutely ill patients. Five are well documented; a favourable response was observed in 4 and an adverse effect was suspected in 1 case. Patients with Lassa fever who have received immune plasma may continue to excrete virus by the respiratory and urinary routes; isolation procedures should remain in effect after transfusion. Further clinical trials and

observations in individual patients receiving serotherapy should be carefully recorded.

Under emergency conditions, the use of convalescent plasma of undetermined potency and safety may be contemplated. The principal hazard is the transfusion of plasma containing Lassa virus to a patient with disease suspected on clinical grounds but not proved to be Lassa fever. Since viraemia has been documented 19 days after onset and the development of antibody is often delayed, plasma to be used for transfusion therapy should never be obtained earlier than 3 weeks after onset and preferably should be obtained 6 weeks or more after onset.

The world's supply of stored immune plasma is very limited. The World Health Organization and others are attempting to identify potential immune donors by serosurveys of hospital workers and missionaries in Africa. A small cadre of cooperative persons willing to undergo plasmapheresis could generate a volume of plasma large enough to allow the preparation of specific immunoglobulin. In the endemo-epidemic region of Sierra Leone, where the need for immunotherapy is at present great, a selective blood donor programme is precluded by the difficulties involved in locating and obtaining blood from specific indigenous immune individuals. Because the prevalence of antibody in the general population may be as high as 10%, an alternative plan is currently under consideration: plasma would be routinely separated from all blood units used for patients with conditions requiring the transfusion of packed red blood cells (e.g., anaemic patients). Potent plasma units, identified by serological tests and screened for hepatitis antigen, would be stored frozen and would be available for use in the endemic region.

TRANSFER AND EVACUATION OF PATIENTS

Since the treatment of patients with Lassa fever requires the use of isolation facilities and advanced clinical resources, evacuation from rural primary-care hospitals to better equipped medical centres within the endemic area or country may be desirable. It seems certain that Lassa fever will be a continuing public health problem in parts of West Africa; health authorities should therefore consider the selection and designation of regional hospitals as Lassa fever treatment centres. These hospitals should be suitably equipped and selected personnel should be trained in isolation techniques and in the management of patients with severe illness.

International air transfer, generally to the country of national origin, has occurred in a number of cases involving expatriates. Precautions taken to avoid cross-contamination of crew and passengers have varied from none to the use of a charter flight and a plane with a specially equipped air-conditioning system. Epidemiologically the use of a special flight is the only acceptable method, though costs are very high. International transfer should be undertaken only with the specific agreement of the health administration and clinical centre of the receiving country. Organizations such as missionary groups and foreign health agencies that have medical personnel stationed in endemic areas should consider in advance their responsibilities to the individuals concerned and to the international community. The need for overseas transfer would be obviated by the establishment of an intensive care unit and immune plasma bank available to nationals and expatriates throughout the whole of West Africa.

RÉSUMÉ

DIAGNOSTIC DE LA FIÈVRE DE LASSA, ET ISOLEMENT ET TRAITEMENT DES MALADES

Le tableau clinique de l'infection due à la fièvre de Lassa couvre un large spectre, allant d'une affection fébrile très bénigne à une longue maladie avec issue fatale. Le diagnostic précoce est essentiel car le virus est transmissible à l'hôpital. Les manifestations cliniques sont d'abord insidieuses avec accès fébrile, frissons, myalgies et céphalées, suivis selon le cas par une pharyngite, des symptômes gastro-intestinaux, de la toux, des douleurs thoraciques, des étourdissements et une diminution de l'ouïe. Chez 35 à 50% des cas hospitalisés, la maladie progresse jusqu'à la forme aiguë, avec toxémie prononcée, syndrome d'épanchement diffus des capillaires, manifes-

tations hémorragiques, troubles respiratoires, perturbation du système nerveux central, oligurie et état de choc.

Il est indispensable de faire un parallèle avec la fièvre typhoïde lors du diagnostic différentiel clinique; l'hémoculture et l'administration de chloramphénicol à titre expérimental peuvent se révéler utiles.

Le diagnostic précoce spécifique dépend de l'isolement du virus dans le sérum, le pharynx, l'urine ou le liquide pleural. Parmi 44 spécimens de sérum recueillis pendant les 14 premiers jours de la maladie, la présence du virus de Lassa a été confirmée dans 36 (82%). Le virus est moins souvent observé, en revanche, dans le pharynx et

l'urine. La virurie peut persister jusqu'à 32 jours, et il est arrivé que des sérums et prélèvements pharyngés soient positifs pendant 19 jours.

Les malades dont les symptômes cliniques permettent de diagnostiquer la fièvre de Lassa doivent être rigoureusement isolés. Dans la pratique, la durée de l'isolement dépend du rétablissement clinique, mais on pourra s'inspirer à cet égard de l'évolution de la virémie et des excréments viraux décrites plus haut. Des problèmes particuliers surgissent quand des spécimens infectieux sont obtenus en vue d'épreuves anatomo-pathologiques cliniques. Pour certaines études, il est possible d'inactiver le virus dans le sérum ou l'urine avant l'épreuve en laboratoire.

Le traitement du malade comportera au premier chef

la surveillance du bilan des liquides organiques dès le début de la phase aiguë et l'on devra veiller aux signes d'instabilité hémodynamique et d'épanchement des capillaires. Le traitement spécifique au plasma immun, qui n'a été essayé que chez quelques malades, semble devoir donner de bons résultats, mais il n'existe que des quantités très faibles de plasma immun.

Du fait que le traitement des cas graves exige des installations cliniques perfectionnées, il peut s'avérer nécessaire de transférer le malade dans un centre médical bien équipé. Il faudra affréter un avion spécial pour transporter les malades dans un autre pays où la fièvre de Lassa n'est pas endémique, afin de réduire le risque d'une contamination croisée.

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DISCUSSION

K. JOHNSON: Your clinical description of Lassa fever and the handling of it correspond exactly to what we see with Junin and Machupo disease. There is a big difference, however, in the viraemia data, and I think this may be one reason why Lassa fever presents such a different problem. In the case of Bolivian haemorrhagic fever, the

virus cannot be isolated from blood of the patients in more than about one in four attempts at any time in the course of the illness. In the care of well over 700 patients, there has never been, in the original focus at least, an instance of transmission to medical personnel. Since then there has been a small outbreak in Cocha-

bama where person-to-person transmission occurred. Lassa fever is exceptional in that such person-to-person transmission occurs frequently.

MAIZTEGUI: I also think that your interpretation of the clinical events in Lassa fever can be applied to both Argentine and Bolivian haemorrhagic fever. However, I would like to add that our recent electron microscopy and immunofluorescent studies in 9 cases of AHF indicate a direct viral pathogenic effect. Finally, I wish to ask how low are the platelet and white cell counts during the acute phase of Lassa fever?

MONATH: The thrombocytopenia is not in the range where one would expect major haemorrhagic problems.

SMITH: Do you think that mobile hospital units might be useful in the treatment of Lassa fever, especially in very remote areas that are relatively inaccessible?

MONATH: This is a question that we could talk about for a long time. I think we have to look at Lassa fever in perspective, keeping in mind the myriad of other health

problems that are much more important in regard to your part of the world than is Lassa fever. I do not believe that it would be desirable to put a lot of money into equipping a mobile unit and so use up resources that are needed to combat diseases like malaria and onchocerciasis; this would be a conceptual mistake. But to alter existing health facilities by establishing isolation rooms and by training existing personnel is a reasonable approach. I am not sure that you will ever be able to reach the villages that are 10 miles off the road or even know that they had a case of Lassa fever in the first place.

SAMA BANYA: ^a In Africa, isolation wards readily become private wards, remote from the main block, and this makes it difficult to provide adequate nursing coverage. It seems better to use barrier nursing on the main wards of the hospital in order to assure that the patients are constantly under care. I also believe that patients with Lassa fever should not be moved at all. Perhaps it would be better to improve the general care of these patients in the areas where the disease is recognized.

^a Kenema, Sierra Leone.